50. (New) The isolated nucleic acid sequence of claim 37 wherein said sequence comprises nucleotides 142-414.

51. (New) The isolated nucleic acid sequence of claim 37 wherein said sequence comprises nucleotides 415-1083.

REMARKS

In the Official Action dated May 8, 2001, the specification has been objected to due to certain alleged informalities. Claim 30 has been objected to under 37 C.F.R. §1.75(c) as allegedly in improper form. Claims 1-2, 7-10, 25 and 28-30 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claims 1-2, 7-10, 25 and 28-30 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support.

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

The specification has been objected to as allegedly containing certain informalities in the Brief Description of the Drawings. Applicants have amended the Brief Description of the Drawings, and in particular Figures 1, 3, 4, 5 and 7 to meet the labeling requirements under 37 C.F.R. §1.84(u)(1). Applicants respectfully acknowledge that certified copies of Application Serial Numbers PN-6135, PN-7276 and PO-2208 remain outstanding. Applicants respectfully submit that certified copies of the foregoing Australian applications are being sought and will be filed in due course.

Claim 30 has been objected to under 37 C.F.R. §1.75(c) as allegedly in improper form. Applicants have amended Claim 30 and added new Claim 36, support for which is found throughout the specification and specifically at Claim 30. Accordingly, Claim 30 complies with the requirements under 37 C.F.R. §1.75(c) and withdrawal of the objection thereto is respectfully requested.

Claims 1-2, 7-10, 25 and 28-30 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. The Examiner specifically alleges that "derivative" has not been defined in the claims nor specification to allow the metes and bounds of the claims to be determined. Applicants specifically direct the Examiner's attention to the specification at Page 29, lines 27-30 which provides a clear definition of "derivatives" which are contemplated to include "... any and all derivatives of NR4 including mutants, parts, fragments, portions, homologues and analogues...". The Examiner's attention is also specifically directed to Example 6 which identifies specific derivatives including both the immunoglobulin-like domain (amino acids 27-117) and the haemopoietin receptor domain (amino acids 118-340) of the extra-cellular region of murine IL-13rα. Both domains are clearly delineated portions and therefore contemplated derivatives of IL-13rα. Moreover, Example 11 describes the cloning of human IL-13rα and the approximate 75% similarity to murine NR4 at the amino acid level. Figure 7 aligns murine and human IL-13rα sequences and clearly demonstrates the similarity between the two sequences. With the sequences aligned, it is apparent that the human immunoglobulin-like domain spans residues 28-118 and human haemopoietin receptor domain spans residues 119-341. Furthermore, the mature form of human IL-13rα (spanning amino acids 26-345 of SEQ ID NO:4) is deducible from

Example 12. Example 12 specifically provides that the murine equivalent of IL-13rα spans amino acids 27-344 of SEQ ID NO:2. Accordingly, Claims 38-51 have been added to further define the subject matter to which applicants are entitled. No new matter has been added.

Claims 28 and 29 have been rejected as allegedly indefinite because it is "not clear what is implied by 'interacts' ". In response, Claims 28 and 29 have been amended to delete the recitation "interacts" in favor of the term "binding" as recommended by the Examiner.

Claim 7 has been rejected allegedly because "low stringency conditions" are not specified. Applicants have amended Claim 7 to recite low stringency conditions under which hybridization is performed. Support for Claim 7 is found throughout the specification and particularly at Example 11, Page 39, lines 26-28.

Claims 2, 7, 10 and 29 have been rejected as allegedly indefinite because of the terms "capable of interacting", "capable of interaction", "capable of directed", and/or "capable of hybridizing" contained in each claim, respectively. In accordance with the Examiner's recommendation and in an effort to expedite favorable prosecution, the terms "capable of" have been omitted from the claims.

Claim 30 has been rejected for depending upon an indefinite base claim. As indicated above, Claim 30 and base Claims 7 and 10 have been amended, thereby obviating the Examiner's rejection.

Accordingly, the rejections of Claims 1-2, 7-10, 25 and 28-30 under 35 U.S.C. §112, second paragraph, are overcome and withdrawal thereof is respectfully requested.

Claims 1-2, 7-10, 25 and 28-30 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. The Examiner concedes that the specification is enabling for an isolated nucleic acid (SEQ ID NO:3) encoding a haemopoietin polypeptide (IL-13) comprising SEQ ID NO:4. However, the Examiner alleges that the "scope of the claims, which encompass other nucleic acid derivatives encoding polypeptides are not enabled by the disclosure". Applicants respectfully submit that the specification teaches the isolation and characterization of murine IL-13rα (SEQ ID NOS:1 and 2) and also the isolation and characterization of human IL-13rα (SEQ ID NOS:3 and 4) using murine probes. The human and murine sequences have a high degree of sequence similarity. The specification also specifically describes sub-domains of the IL-13rα molecule and teaches the preparation of soluble IL-13rα lacking the transmembrane and cytoplasmic domains (see e.g., Example 6, 11 and 12).

The Examiner has alleged that the specification does not provide support for "derivatives" of SEQ ID NOS:3-4. Notably, the Examiner readily admits and has reiterated that "derivatives of IL-13 can be made [according to the teachings of the specification]". Consistent with that acknowledgement, applicants have identified specific functional derivatives of IL-13rα and a structural basis (i.e., the sequences) from which the skilled artisan can readily prepare such derivatives without undue experimentation. Thus, derivatives of IL-13rα are disclosed and enabled in accordance with the provisions of 35 U.S.C. §112, first paragraph.

Claim 25 has been rejected based on an alleged failure of the specification to enable one skilled in the art to make and/or use the pharmaceutical composition encompassed

by the claim. The Examiner alleges that "neither the specification nor the prior art provides sufficient guidance as to what specific diseases can be treated by administering a pharmaceutical composition comprising the composition of Claim 25". In an effort to expedite favorable prosecution, Claim 25 has been amended to delete the recitation "pharmaceutical". Accordingly, the rejections of Claims 1-2, 7-10, 25 and 28-30 under 35 U.S.C. §112, first paragraph, are overcome and withdrawal thereof is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Thus, in view of the foregoing amendments and remarks, applicants respectfully submit that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Please replace the paragraph beginning at Page 31, Lines 10-22 with the following rewritten paragraph:

[BRIEF DESCRIPTION OF THE FIGURES] BRIEF DESCRIPTION OF THE DRAWINGS

[Figure 1 is a representation of] Figures 1A-1F show the nucleotide [SEQ ID NO:1] and predicted amino [SEQ ID NO:2] sequence of murine NR4. The untranslated region is shown in lower case and the translated region in upper case. The conventional one-letter code for amino acids is employed, potential asparagine linked glycosylation sites are underlined and the conserved cysteine residues and WSXWS motif of haempoietin receptor family members are shown in bold. The predicted signal sequence is underlined in bold while the transmembrane domain is underlined with dashes. The sequence shown is a composite derived from the analysis of 8 cDNA clones derived from 3 libraries. The 5'-end of the sequence (nucleotides –60 to 351) is derived from a single cDNA clone but is also present in genomic DNA clones that have been isolated. Boxed region – typical haempoietin receptor domain, amino acids 118-340.

Please replace the paragraph beginning at Page 31, Lines 27 – Page 32, Line 1 with the following rewritten paragraph:

Figure 3 is a graphical representation depicted saturation isotherms of ^{125}I-IL-13 and ^{125}I-IL-4 binding; saturation isotherms depicted as Scatchard plots of IL-4(°) and IL-13(•) binding to (Figure 3 [(]A) COS cells expressing the IL-13Rα(NR4), (Figure 3[(]B) CTLL cells and (Figure 3[(]C) CTLL cells expressing the IL-13Rα(NR4). Data have been

normalized to 1 x10^4 COS cells and 1x10^6 CTLL cells and binding was carried out on ice for 2 to 4 hours.

Please replace the paragraph beginning at Page 32, Lines 3 – 8 with the following rewritten paragraph:

Figure 4 is a graphical representation showing specificity of IL-4 and IL-13 binding; the ability of IL-4(°) and IL-13(•) to compete for ^{125}I-IL-13 binding to (Figure 4[(]A) COS cells expressing the IL-13Rα(NR4) and (Figure 4[(]C) CTLL cells expressing the IL-13Rα (NR4) or to compete for ^{125}I-IL-4 binding to (Figure 4[(]B) CTLL cells and (Figure 4[(]D) CTLL cells expressing the IL-13Rα(NR4). Binding was carried out a 4°C for 2 to 4 hours and the data expressed as a percentage of the specific binding observed in the absence of a competitor (▵).

Please replace the paragraph beginning at Page 32, Lines 10 – 14 with the following rewritten paragraph:

Figure 5 is a graphical representation showing factor dependent proliferation of cells expressing NR4. Two hundred (Figure 5[(]A) CTLL cells or (Figure 5[(]B) CTLL cells expressing the IL-13Rα (NR4) were incubated in the absence of cytokine or with various concentrations of IL-2 (□), IL-4(°) or IL-13 (•). After 48 hours viable cells were counted and data were expressed as a percentage of the number of viable cells observed with a maximal concentration of IL-2.

Please replace the paragraph beginning at Page 32, Lines 3 – 8 with the following rewritten paragraph:

[Figure 7 is a representation of] Figures 7A-7J show the nucleotide and corresponding amino acid sequence of murine and human NR4 (IL-13Rα)genes. The

nucleotide and predicted amino acid sequence of human (H) and murine (M) IL-13Rα(NR4) were aligned by eye, with gaps (-) inserted to optimize the alignment. The numbering is for the murine clone, nucleotides that form part of the coding region are shown in upper case, whilst those of the untranslated regions are shown in lower case. Amino acids identical between the predicted murine and human proteins are indicated by (*). DNA encoding the murine signal sequence is underlined, with A26 or T27 being the predicted first amino acid of the mature protein.

IN THE CLAIMS:

1. (Twice Amended) An isolated nucleic acid molecule comprising [SEQ ID NO:1 or] SEQ ID NO:3 encoding a haemopoietin receptor comprising an amino acid sequence set forth in [SEQ ID NO:2 or] SEQ ID NO:4 or a derivative of said receptor.

2. (Twice Amended) An isolated nucleic acid molecule comprising [SEQ ID NO:1 or] SEQ ID NO:3 encoding a haemopoietin receptor comprising an amino acid sequence as set forth in [SEQ ID NO:2 or] SEQ ID NO:4 or a derivative thereof, wherein said receptor:

(iii) [is capable of interaction] binds with IL-13 or its derivatives; and

(iv) [is capable of interaction] binds with a complex between IL-4 and IL-4 receptor α-chain.

7. (Twice Amended) An isolated nucleic acid molecule comprising a sequence of nucleotides which encodes an IL-13 receptor α-chain or a derivative thereof, said nucleic acid molecule having a nucleotide sequence as set forth in [SEQ ID NO:1 or] SEQ ID NO:3 or a nucleic acid molecule which [is capable of hybridizing] hybridizes to the nucleotide

sequence as set forth in [SEQ ID NO:1 or] SEQ ID NO:3 under low stringency conditions, wherein said low stringency conditions comprise 6x SSC, 0.1% w/v SDS at 42°C.

8. (Twice Amended) An isolated nucleic acid molecule comprising a sequence of nucleotides which encodes an IL-13 receptor α-chain or a derivative thereof having an amino acid sequence as set forth in [SEQ ID NO:2 or] SEQ ID NO:4.

10. (Twice Amended) An expression vector comprising a nucleic acid molecule according to claim 1 or 7 operably linked to a promoter [capable of directing] which directs expression of said nucleic acid molecule in a host cell.

25. (Twice Amended) A [pharmaceutical] composition comprising a nucleic acid molecule according to claim 1 or 2 or 7 or 8 and a pharmaceutically acceptable carrier.

28. (Twice Amended) A method of producing a recombinant polypeptide having at least two of the following characteristics:

(v) comprises an amino acid sequence as set forth in [SEQ ID NO:2 or] SEQ ID NO:4[:];

(vi) is encoded by a nucleotide sequence as set forth in [SEQ ID NO:1 or] SEQ ID NO:3;

(vii) [interacts] binds with IL-13 or its derivatives; and

(viii) said polypeptide, when expressed in COS cells, has a molecular weight of from about 50,000 to about 70,000 daltons as determined by Western blot analysis,

said method comprising culturing cells comprising the expression vector according to claim 10 for a time and under conditions sufficient to express the nucleic acid molecule in said expression vector to produce a recombinant polypeptide and isolating said recombinant polypeptide.

29. (Twice Amended) A method of producing a recombinant polypeptide having at least three of the following characteristics:

(i) comprises an amino acid sequence as set forth in [SEQ ID NO:2 or] SEQ ID NO:4;

(ii) is encoded by a nucleotide sequence as set forth in [SEQ ID NO:1 or] SEQ ID NO:3;

(iii) [interacts] binds with IL-13 or its derivatives;

(iv) said polypeptide, when expressed in COS cells, has a molecular weight of from about 50,000 to about 70,000 daltons as determined by Western blot analysis;

(v) comprises an amino acid sequence derived from IL-4 receptor α-chain; and

(vi) is capable of interaction with IL-13 which is competitively inhibited by IL-4 in cells which express an IL-4 receptor α-chain,

said method comprising culturing cells comprising the expression vector according to claim 10 for a time and under conditions sufficient to express the nucleic acid molecule in said expression vector to produce a recombinant polypeptide and isolating said recombinant polypeptide.

30. (Twice Amended) [An isolated and purified animal] A host cell which expresses the recombinant polypeptide produced by the method according to claim 28 [or 29].

Please add the following new Claims:

36. (New) A host cell which expresses the recombinant polypeptide produced by the method according to claim 29.

37. (New) An isolated nucleic acid molecule comprising a nucleotide sequence set forth in SEQ ID NO:3.

38. (New) An isolated nucleic acid molecule comprising the sequence of nucleotides which encodes an extracellular domain of a haemopoietin receptor comprising an amino acid sequence set forth in SEQ ID NO:4.

39. (New) The isolated nucleic acid molecule of claim 38 wherein said extracellular domain is an immunoglobulin-like domain.

40. (New) The isolated nucleic acid molecule of claim 38 wherein said extracellular domain is an haemopoietin receptor domain.

41. (New) The isolated nucleic acid molecule of claim 39 wherein said immunoglobulin-like domain comprises amino acids 28-118.

42. (New) The isolated nucleic acid molecule of claim 40 wherein said haemopoietin receptor domain comprises amino acids 119-341.

43. (New) The isolated nucleic acid molecule of Claim 37, encoding a polypeptide comprising amino acids 26-345.

44. (New) The isolated nucleic acid molecule of Claim 37, encoding a polypeptide comprising amino acids 26-426.

45. (New) A host cell which expresses the haemopoietin receptor encoded by SEQ ID NO:3.

46. (New) The host cell of any one of claims 30, 36 or 45 wherein said host cell is an animal cell.

47. (New) A method of producing a recombinant polypeptide comprising culturing cells comprising the expression vector according to claim 10 for a time and under conditions sufficient to express a polypeptide encoded by the nucleic acid molecule as set forth in SEQ ID NO:3 in said expression vector and isolating said recombinant polypeptide.

48. (New) The isolated nucleic acid sequence of Claim 37 wherein said sequence comprises nucleotides 136-1095.

49. (New) The isolated nucleic acid sequence of claim 37 wherein said sequence comprises nucleotides 136-1338.

50. (New) The isolated nucleic acid sequence of claim 37 wherein said sequence comprises nucleotides 142-414.

51. (New) The isolated nucleic acid sequence of claim 37 wherein said sequence comprises nucleotides 415-1083.